418  Titin mutations and female sex characterize dilated cardiomyopathy in the elderly

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Aims: Dilated cardiomyopathy (DCM) is frequently caused by genetic factors. Studies identifying deleterious rare variants have predominantly focused on early-onset cases, and little is known about the genetic underpinnings of the growing numbers of patients with DCM who are diagnosed after 60 years of age (i.e., late-onset DCM). The aim is to investigate the prevalence, type, and prognostic impact of disease-associated rare variants in late-onset DCM patients.

Methods and results: We analysed a population of late-onset DCM patients who had undergone genetic testing in seven international tertiary referral centres worldwide. A positive genotype was defined as the presence of “pathogenic” or “likely pathogenic” (P/LP) variants. The study outcome was all-cause mortality. 184 patients over age 60 years (56 females, mean age 67 ± 6 years, mean left ventricular ejection fraction 32 ± 10%) were studied. Sixty-six patients (36%) were carriers of a P/LP variant. Titin truncating variants (TTNtv) were the most prevalent (present in 25% of the total population and accounting for 6% of all genotype-positive patients). During a median follow-up of 42 months (interquartile range: 10–115), 23 patients (13%) died; 17 of these (25%) were carriers of P/LP variants while six patients (5.1%) were genotype-negative (P < 0.001).

Conclusions: In the largest series worldwide, to date, of patients with late-onset DCM, we found a high prevalence of female sex and a high genetic mutation burden, largely due to TTNtv. Patients with a positive genetic test had higher mortality than genotype-negative patients. These findings support the extended use of genetic testing also in the elderly.